a trait DNA molecule which has a length that is insufficient to independently impart a desired trait to plants transformed with said trait DNA molecule and

a silencer DNA molecule effective to achieve post-transcriptional gene silencing and operatively coupled to said trait DNA molecule, wherein said trait DNA molecule and said silencer DNA molecule are heterologous to each other and collectively impart the trait to plants transformed with said DNA construct and wherein at least one of said trait DNA molecule or said silencer DNA molecule is not endogenous to a plant.

REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1, 19, and 46-81 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

The basis for this rejection is the U.S. Patent and Trademark Office's ("PTO") view that undue experimentation would be required to determine the length of a trait DNA molecule which is insufficient to independently impart that trait and the length of a silencer DNA molecule which, when coupled to such a trait DNA molecule, would permit that trait to be imparted. Applicants disagree with this position.

As to the trait DNA molecule length, the present application teaches a procedure which would fully permit one of ordinary skill in the art to practice the present invention. Examples 1-5 teach how to prepare constructs containing different lengths of the N (i.e. nucleocapsid encoding) gene from Tomato Spotted Wilt Virus, transforming plants with these constructs, and determining whether the resulting plants are resistant or susceptible to that virus. From this disclosure, one of ordinary skill in the art, through routine experimentation, would be fully able to make constructs with fragments from other trait DNA molecules and test whether those fragments have a length sufficient to independently impart that trait to a plant. Accordingly, applicants submit that the present invention is fully enabling with regard to the trait DNA molecule.

The purpose of the silencer DNA molecule is to effect post-transcriptional gene silencing. As described above, a trait DNA molecule in accordance with the present

invention can be identified by routine experimentation. With this trait DNA molecule established, it would be well within the abilities of one of ordinary skill in the art to identify silencer DNA molecules in accordance with the present invention. Examples 6-7 teach fusing a GFP encoding gene to N gene fragments, transforming such constructs into plants, and testing whether the plants are resistant. From this disclosure, one of ordinary skill in the art would be fully able to identify, through routine experimentation, other suitable silencer DNA molecules to practice the present invention. Examples of useful silencer DNA molecules are described in the second full paragraph on page 18 of the present application.

Since one of ordinary skill in the art would be fully able to make and use the present invention, the lack of enablement rejection under 35 U.S.C. § 112 (1st para.) should be withdrawn.

The rejection of claims 1, 19, and 46-81 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed.

Claim 1 has now been amended to state that the silencer DNA molecule is "effective to achieve post-transcriptional gene silencing". As stated in the paragraph bridging pages 18 and 19, this concept is utilized in conjunction with the present invention as follows:

> While not wishing to be bound by theory, by use of the construct of the present invention, it is believed that post-transcriptional gene silencing is achieved. More particularly, the silencer DNA molecule is believed to boost the level of heterologous RNA within the cell above a threshold level. This activates the degradation mechanism by which viral resistance is achieved.

From this passage, the purpose of the claimed silencer DNA molecule would be apparent to one of ordinary skill in the art. Suitable forms of such DNA molecules are wide ranging. For example, as set forth in the paragraph bridging pages 17 and 18 of the present application, the DNA molecule of the present invention can be in the sense or anti-sense orientation.

Claim 1 further calls for the trait DNA molecule and the silencer DNA molecule to "collectively impart the trait to plants transformed with said DNA construct". There is no requirement that applicants provide the theory by which such trait is imparted. However, the claimed invention does indicate that the silencer DNA molecule is effective to

achieve post-transcriptional gene silencing. Applicants submit that this is more than sufficient to make the claimed invention clear to one of ordinary skill in the art.

For all of these reasons, the rejection under 35 U.S.C. § 112 (2nd para.) should be withdrawn.

The rejection of claims 1, 19, 59, 63-65, and 67-69 under 35 U.S.C. § 102 as anticipated by Seymour et. al., "Down-Regulation of Two Non-Homologous Endogenous Tomato Genes With a Single Chimeric Sense Gene Construct," Plant Molecular Biology 23: 1-9 (1993)("Seymour") is respectfully traversed.

Seymour transforms tomato with a gene construct which includes a gene having 1320 base pairs and encoding the full length pectinesterase ("PE") enzyme fused to a 244 base pair gene fragment encoding the N-terminus of the polygalacturonase ("PG") enzyme. The construct ("PGPE") is positioned between the CaMV 35S promoter and terminator. When this construct was transformed into tomato, it was found that expression of the endogenous tomato PG and PE genes, as well as the PGPE gene, were inhibited in the tomato fruit. Thus, Seymour was able to down-regulate the endogenous PG and PE genes with his construct containing a PGPE transgene.

As noted above, the claimed silencer DNA molecule is effective to achieve post-transcriptional gene silencing. There is no mention in Seymour that this phenomenon is utilized. In order to show otherwise, Seymour would have had to determine which genes are silenced, which genes are not silenced, and which genes that are not silenced alone become silenced when linked with another gene. In order to have any relevance to the present invention, Seymour's 244 base pair PG gene fragment needs to be viewed as the claimed trait DNA molecule. However, there is no indication in Seymour that the PG fragment used by Seymour is of insufficient length to independently impart its trait to a plant which has been transformed with that fragment. To determine if this were so, Seymour would have had to make transgenic plants with that fragment in them and test whether that plant possessed the trait imparted by the PG fragment. Seymour did none of this. There is also no indication that the full PE gene used by Seymour is effective to achieve post-transcriptional gene silencing, as claimed. In any event, the PE and PG genes used by Seymour are from tomato and, therefore, fail to meet the claim limitation that "at least one of said trait DNA molecule or said silencer DNA molecule is not endogenous to a plant." There is no suggestion that the teachings of Seymour have any relevance to using genes not endogenous to a plant. Finally,

Seymour also fails to teach the use of multiple trait genes, as set forth in claims 19, 47, 59, and 71.

In view of all of these deficiencies in Seymour, the anticipation rejection based on this reference should be withdrawn.

The rejection of claims 46-47, 51-58, 70-71, 75, and 78-81 are rejected under 35 U.S.C. § 102 as anticipated by Seymour is respectfully traversed for substantially the same reasons set forth above.

The rejection of claims 1, 19, and 58-59 under 35 U.S.C. § 103 for obviousness over Seymour in view of WO 94/16550 to Gonsalves et. al., ("Gonsalves") is respectfully traversed.

Gonsalves teaches making transgenic plants containing the nucleocapsid nucleotide sequence from tomato spotted wilt virus ("TSWV") to confer resistance to Tospoviruses. There is no suggestion in Gonsalves of using a trait DNA molecule and a silencer DNA molecule which are heterologous to each other (i.e. the trait and silencer DNA molecules are from different genes). It is the PTO's position that it would have been obvious to one of ordinary skill in the art to replace the PE and PG genes in Seymour's construct with 2 of the nucleotide sequences taught by Gonsalves.

Applicants submit that there would have been no motivation to combine the teachings of Seymour and Gonsalves. Seymour is working with the PE gene and the PG gene fragment, both of which come from tomato, to achieve down-regulation of endogenous genes in tomato. By contrast, Gonsalves seeks to impart disease resistance to plants by inserting genes from a plant virus into such plants. There is no suggestion in either Seymour, Gonsalves, or the art in general of why the down regulation phenomena of Seymour would have any relevance to Gonsalves' technique of imparting resistance to plants by inserting viral genes into the plants. As a result, one of ordinary skill in the art would have no reason to combine the features of these references as suggested in the outstanding office action.

Even if, assuming *arguendo*, the combination of Seymour and Gonsalves were proper, which it is not, that combination would not teach the present invention. As noted above, the present invention is directed to "a trait DNA molecule which has a length that is insufficient to independently impart a desired trait to plants transformed with said trait DNA molecule" and a silencer DNA molecule which is "effective to achieve post-transcriptional gene silencing". Even when the features of Seymour and Gonsalves are combined, the

combination of these references fails to suggest either of these concepts. Although Gonsalves imparts disease resistance with less than full length viral genes, this is achieved with viral genes having half the length of full length genes; as shown in Table 1 of the present application (page 30), shorter lengths are ineffective in themselves imparting resistance. In view of this deficiency in such shorter fragments, there would have been no reason to use them when attempting to impart disease resistance. There is also no teaching of a silencer DNA molecule in either Seymour or Gonsalves, let alone its use to impart a trait to transgenic plants where the trait DNA molecule has a length which alone is insufficient to independently impart that trait. Thus, the combination of Seymour and Gonsalves fails to teach the claimed invention.

For all of these reasons, the rejection based on the combination of Seymour and Gonsalves should be withdrawn.

The rejection of claims 46-57 and 70-81 under 35 U.S.C. § 103 for obviousness over Seymour is respectfully traversed for substantially the same reasons set forth previously.

In view of all of the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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